

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 February 2005 (03.02.2005)

PCT

(10) International Publication Number
WO 2005/009510 A2

(51) International Patent Classification⁷: **A61M**

(21) International Application Number:
PCT/US2004/023634

(22) International Filing Date: 21 July 2004 (21.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/560,717 23 July 2003 (23.07.2003) US

(71) Applicant (for all designated States except US): **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, 5th floor, Oakland, CA 94602-5200 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MITRAGOTRI,**

Samir [IN/US]; 6821 Sweetwater Way, Goleta, CA 93117 (US). **KARANDE, Pankaj** [IN/US]; 467 Cole Place, Goleta, CA 93117 (US). **JAIN, Amit, K.** [US/US]; 6657 El Colegio, #5, Goleta, CA 93117 (US).

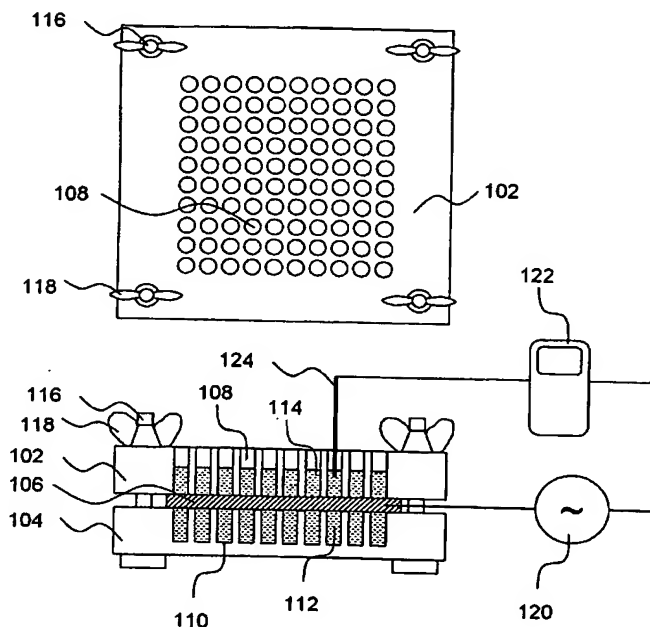
(74) Agent: **BERLINER, Robert**; Fulbright & Jaworski L.L.P., 865 South Figueroa, 29th floor, Los Angeles, CA 90017-2571 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: **PENETRATION ENHANCER COMBINATIONS FOR TRANSDERMAL DELIVERY**



(57) Abstract: A high throughput screening and isolation system identifies rare enhancer mixtures from a candidate pool of penetration enhancer combinations. The combinations are screened for high penetration but low irritation potential using a unique data mining method to find new potent and safe chemical penetration enhancer combinations. The members of a library of chemical penetration enhancer combinations are screened with a high throughput device to identify "hot spots", particular combinations that show higher chemical penetration enhancement compared to neighboring compositions. The irritation potentials of the hot spot combinations are measured to identify combinations that also show low irritation potential. A active component, such as a drug, is then combined with the combination in a formulation which is tested for the ability of the drug to penetrate into or through skin. It is then assessed whether the formulation can deliver the quantity of drug required, and animal tests are conducted to confirm *in vivo* the ability of the chemical penetration enhancer

combinations to facilitate transport of sufficient active molecules across the skin to achieve therapeutic levels of the active molecule in the animal's blood. The invention provides specific unique and rare mixtures of chemical penetration enhancers that enhance skin permeability to hydrophilic macromolecules by more than 50-fold without inducing skin irritation, such as combinations of sodium laurel ether sulfate and 1-phenyl piperazine, and combinations of N-lauryl sarcosine and Span 20/sorbitan monolaurate.

BEST AVAILABLE COPY

WO 2005/009510 A2



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.